Severity factors of Acquired Pneumonia Community in a children's hospital in the Colombian Caribbean

Factores de severidad de Neumonía Adquirida en la Comunidad en un hospital infantil del Caribe colombiano

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Abstract

***Objective**: To identify predisposing factors to developing severe pneumonia in hospitalized children diagnosed with community-acquired pneumonia hospitalized in Cartagena's Napoleón Franco Pareja children's Hospital.*
***Methods**: Analytical observational cross-sectional study performed in patients under 18 years. Data from surveys and records were analyzed. Univariate and bivariate analysis was performed. The variables are grouped according to the presence or absence of complications and analyzed by ji-square test. We calculated OR of each of the dummy variables to evaluate their association with complications. A P < 0.05 was considered statistically significant for all analyses.*
***Results**: 301 patients with severe pneumonia were included. Risk factors related to severity: age less than 3 months (OR: 4.86; CI 95%: 1,5 - 14.3; p = 0.004); exclusive breastfeeding for less than 6 months (CI:95% 7,7- 1,4; p = 0.0019); heart disease (OR: 5.37; CI 95%: 1,28- 19,88, p = 0.010); prematurity (OR: 1.62, CI 95%: 0.93- 6.69, p = 0.034); Incomplete vaccination (OR: 2.32; CI: 95% 1.07 - 5.10; p = 0.015).*
***Conclusions**: It was found increased severity risk, statistically significant, in patients less than 6 months breastfeeding, prematurity, heart disease, incomplete vaccination scheme, and positive blood culture with Sp. pneumonia*

Keywords: pneumonía, tachypnea, Streptococcus pneumoniae.

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Resumen

***Objetivo**: Identificar factores predisponentes a desarrollar neumonía severa en niños hospitalizados con diagnóstico de NAC en el Hospital Infantil Napoleón Franco Pareja de Cartagena Colombia.*
***Materiales y métodos**: Estudio observacional transversal analítico en pacientes menores de 18 años hospitalizados con neumonía adquirida en la comunidad. Se analizaron datos obtenidos de encuestas y registros clínicos. Se realizó un análisis descriptivo univariado y bivariado. Las variables se agruparon según la presencia o no de complicación y se analizaron a través de la prueba ji cuadrado. Se realizó el cálculo de OR de cada una de las variables dicotómicas para evaluar su asociación a complicaciones. Una P<0,05 fue considerada como estadísticamente significativa para todos los análisis.*
***Resultados**: Se incluyeron 301 pacientes con neumonía grave. Los factores de riesgo más relacionados con severidad fueron: edad menor de 3 meses (OR: 4,86; IC 95%: 1,5- 14,3; p 0,004); la lactancia materna exclusiva menor a 6 meses (IC 95%: 1,4- 7,7; p 0,0019); cardiopatía (OR: 5,37; IC 95%: 1,28- 19,88; p: 0,010); prematurez (OR: 1,62; IC: 0,93-6,69; p: 0,034); esquema incompleto de vacunación (OR: 2,32; IC 95%: 1,07-5,10: p: 0,015).*
***Conclusiones**: Se encontró aumento de riesgo de severidad en pacientes con lactancia materna menor de 6 meses, prematurez, cardiopatía, esquema de vacunación incompleto, y hemocultivo con Sp. Neumoniae positivo.*

Palabras clave: neumonía, taquipnea, Streptococcus pneumoniae.

INTRODUCTION

Acquired Pneumonia in the Community (CAP) is the leading cause of death in children under 5 years of age in the world, with about 1.2 million cases in 2015 (1). The most vulnerable population is found in the developing countries, especially children under 1 year old, in whom the severe form of this entity prevails, increasing in them the risk of death (2, 3). This is due to socioeconomic conditions, difficulties in access and quality of healthcare services, malnutrition and low vaccination coverage (4, 5).

Every year between 140 and 160 million new CAP's cases are reported, with a lethality of 4% in hospitalized patients and 1% in outpatient (6). According to WHO, each year one of each 20 children under 5 years will have an episode of pneumonia, and of these, one to four of every thousand will require hospitalization (7, 8). In 2010, 120 million episodes of pneumonia were estimated in children under 5 years old, of whom 1.3 died (81% in the first 2 years of life) (1). Streptococcus pneumoniae (Sp) is responsible for 18.3% of these cases (9, 10) CAP was confirmed in children under 3 years old by this germ, in Latin America: a rate of 55 per 100,000 children in Brazil and 76 per 100,000 children in Bogota, Colombia, in 2012 (11).

Risk factors have been described to develop severe pneumonia (12). Among these we find: low birth weight(13, 14), prematurity (15, 16), being younger than 3 months old (17), breastfeeding not exclusive (18), teenager or unlearned mother (19), meeting at day-care centers, overcrowding, malnutrition (20, 21), immunocompromised, presence of congenital heart disease or chronic lung disease (17), exposure to cigarette smoke or biomass (22), incomplete vaccines schedule (23), late medical care (24), and others (15, 24, 25). WHO seeks to reduce the morbidity and

mortality caused by CAP through the identification and dissemination of these factors (12).

There are no studies in our population that determine the vulnerability of some children with CAP to develop complications. The main objective of this study is to identify predisposing risk factors to develop severe pneumonia in hospitalized children diagnosed with community-acquired pneumonia in the Colombian Caribbean.

Methods

An analytical cross-sectional observational study was realized that looked to identify predisposing factors to develop severe pneumonia in hospitalized children diagnosed with CAP in the Napoleón Franco Pareja Children's Hospital (HINFP) between January and December 2014.

Study Subjects

It was included Children younger than 18 years old of both sex with a diagnosis of CAP according to definitions of WHO, British's Chest Society and American Society of Infectious Diseases; who were admitted at emergency service (15-17) and were hospitalized for more than 24 hours. Children admitted to Intensive Care Unit (ICU) from another institution, and patients forwarded to another institution without observable evolution were excluded.

Data collection and statistical analysis

A form was designed that included clinical record's information and the interview with parents and / or caregivers with prior informed consent. Socioeconomic variables (table 1), epidemiological variables (table 2), clinics (signs and symptoms, complications, hospital staying, oxygen therapy, condition at departure, paraclinical record) were included.

Table 1. Socioeconomic Profile of patients with CAP in the Napoleón Franco Pareja Children's Hospital (HINFP) in 2014

Total (n):	301
Age:	
(Half); SD	(2,52); 2,90
[Median]	[1.57]
[Rank]	[.0739726 - 15.21096]
Sex:	
Male n; (%)	159, (52,82%)
Social Security:	
Contributory (%)	6 (1,99 %)
Particular (%)	3 (1%)
Subsidized (%)	286 (95,02 %)
Linked (%)	6 (1,99%)
Socioeconomic:	
Stratum 1 (Low-Low)	236 (78.41%)
Stratum 2 (Low)	50(16.61%)
Stratum 3 (Medium-Low)	15 (4.98%)
Geographic Location (Provenance)	
Urban (%)	257(85,38%)
Rural (%)	44(14,62%)
Condition of overcrowding (%):	109(36,21%)
Maternal age in years:	
(Half); SD	(23.64); 5,79
[Median]	[22]
[Rank]	[15 - 48]
Maternal Education:	
Without education	3 (1%)
Primary	28(9,3%)
High school	223 (74,09%)
Higher	47 (15,61%)

The data were integrated into a spreadsheet for MS Excel 2010™. The statistical package Stata 11 was used to analyze the information. Categorical variables were measured in percentages and continuous variables were measured with central tendency and dispersion's measure. Contingency tables were used as a measure of association between categorical variables, measuring their

statistical significance with the chi-square test and the exact Fisher test for small frequencies. The Relative Risk (RR) of each factor and its confidence interval were calculated. All the statistical tests were contrasted with a level of significance of 5%.

Table 2. Epidemiological profile of patients with CAP hospitalized in HINFP in 2014.

	N	%
Personal history:		
Asthma	104	34,6
Allergies	15	5,0
Diabetes	3	1,0
Down	1	0,3
Sickle cell anemia	11	3,7
Cardiopathy	13	4,3
Prematurity	35	11,6
Hospitalized last month by CAP	11	3,7
Exposure to fumes	63	20,9
Smoke	28	9,3
Exposure to painting	8	2,7
Malnutrition	18	6,0
Others*	38	12,6
Vaccination scheme **		
Full Pentavalent + DPT Vaccination	239	79,4
S. pneumoniae Vaccination	240	79,7
Influenza Vaccination	234	77,7

*1 Case of: Tuberculosis, Cholelithiasis, Cystic Fibrosis, Cleft Lip, Bronchopulmonary Dysplasia, Esophageal Atresia, Ulcerative Colitis, Thalassemia, Myelomeningocele, Osteosarcoma, Esophageal Atresia and S. De Moebius. 2 Cases of: Recurrent Pneumonia, Gastroesophageal Reflux, Cerebral Palsy. 3 Cases of: Tracheostomy and Epilepsy.
** Vaccination scheme verified by card.

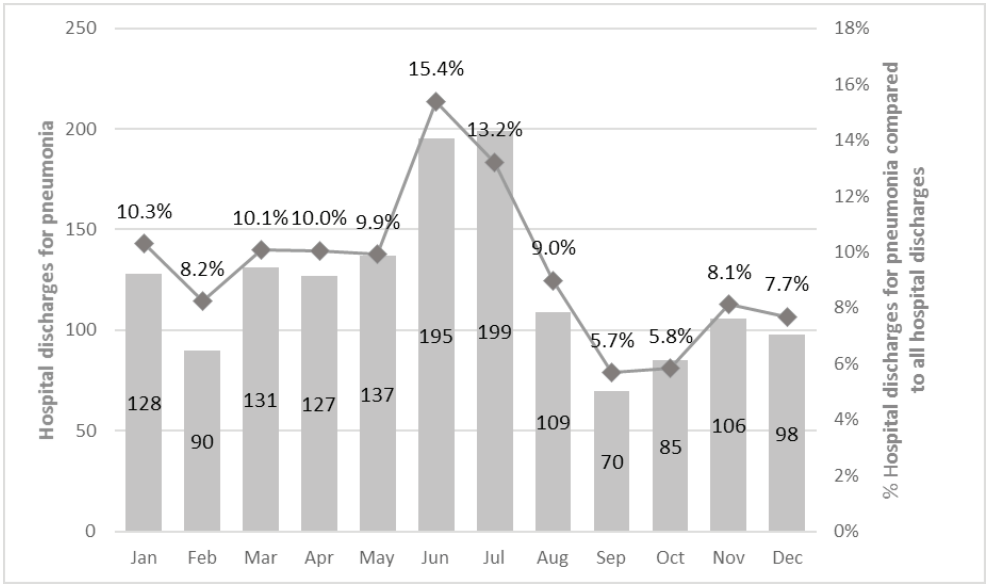
Ethical issues

According to the resolution 008430 of 1993, the then Ministry of Health, the study was categorized safe and approved by the Cartagena University's Medicine faculty's research department.

Results

There were 15,546 discharges at HINFP in 2014; of which 1,475 (9.5%) were diagnosed with pneumonia (Graph 1); Of these, 325 patients with diagnosis of CAP were selected. 301 (20.4%) met the inclusion criteria. The reasons for exclusion were: 8 for incomplete data; 4 did not meet definition of NAC; 1 was over 18 and 11 were under 24 hours.

Tables 1 and 2 summarize the socioeconomic and epidemiological characteristics of the subjects studied. There were no differences regarding sex. The average age in years was 2.5 (SD: 2.9) and the median was 1.5 with IQR (0.07 - 15.2). 85.3% came from urban areas and 78.4% had socioeconomic strata 1. 95% of patients were in a subsidized regime of social security. The median age of the mother was 22 years (IQR: 15 - 48). The most frequent clinical antecedents were asthma, prematurity, exposure to smoke, presence of allergies and heart disease. 79.4% had a complete vaccination scheme for pentavalent and DPT; 79.7% for pneumococcus and 77.7% for influenza.



Fuente:

Graphic 1. Proportion of disbursements by NAC with respect to the total of disbursements in Napoleón Franco Pareja Children's Hospital Foundation in 2014

Clinical profile

50% of the patients consulted on the third day after the onset of symptoms (average of 4.1 days, SD: 3.4). The average stay was 6.0 days (SD: 5.5 and range: 1-56 days). In the general ward, the average stay was 5.0 days (SD: 3.9) and in the ICU it was 9.2 (SD: 5.2). Cough, respiratory distress, rhinorrhea, abdominal pain and vomiting were the most frequent initial symptoms. 69.1% of the patients presented tachypnea and 66.4% of these had chest wall indrawing. Oxygen therapy was required in 138 patients (45.8%); of these, 18.8% required mechanical ventilation. The most used antibiotic schemes were: penicillin (63.8%); ceftriaxone (16.3%); ceftriaxone / clindamycin (5.0%). Two deaths were recorded in the group, in which one had malnutrition and the other sepsis as a complication (Table 3).

Table 3. Clinical profile hospitalized with NAC in HINFP in 2014

	n= 301	%
Signs and symptoms:		
Fever	258	85,7
Cough	245	81,4
Respiratory difficulty	208	69,1
Rhinorrhea	97	32,2
Abdominal pain	27	9,0
Vomit	17	5,7
Tachypnea	208	69,1
Chest wall indrawing	200	66,5
Oxygen Support:		
Oxygen requirement	138	45,9
Mechanic ventilation	26	18,84
Hospitalization room		
General room	267	88,7
ICU	34	11,3
Final Condition		
Alive	299	99
Dead	2	1,0

Patients were classified as presenting severe pneumonia (88.7%) and very severe pneumonia (11.3%). 44 (14,6%) of the patients presented complications; Of these, 7.5% had severe pneumonia and 70.6% had very severe pneumonia, the statistical difference was significant (p = 0.000). The most frequent complication in the group of severe pneumonia was pleural effusion (5.6%) and in the group of very severe pneumonia, sepsis (52.94%). Some patients presented several antecedents (table 4).

Table 4. Frequency of complications in patients with NAC hospitalized at the Napoleón Franco Pareja Children's Hospital in 2014

CAP	TOTAL N=301	CAP Severe N=267 (88,7%)	CAP Very severe N=34 (11,3%)	Pr (Z < z)
Complications	44 (14,6%)	20 (7,5%)	24 (70,6%)	0.000
Pleural effusion	22 (7,3%)	15 (5,6%)	7 (20,6%)	0.001
Sepsis	20 (6,6%)	2 (0,7%)	18 (52,9%)	0.000
Atelectasis	5 (1,6%)	2 (0,7%)	3 (8,8%)	0.000
Empiema	2 (0,6%)	1 (0,4%)	1 (2,9%)	0.041
Pulmonary abscess	1 (0,3%)	0 (0,0%)	1 (2,9%)	0.003
Pneumothorax	1 (0,3%)	0 (0,0%)	1 (2,9%)	0.003
Pulmonary hypertension	1 (0,3%)	0 (0,0%)	1 (2,9%)	0.003

Risk factors of severity

Table 5 shows the risk factors and their association with severe pneumonia. The most related to severity are: age less than 3 months (OR: 4.8, 95% CI: 1.5- 14.3, p 0.004); exclusive breastfeeding less than 6 months (95% CI: 1.4-7.7, p 0.0019); heart disease (OR: 5.4, 95% CI: 1.3- 19.9, p: 0.010); prematurity (OR: 1.6, CI: 0.9-6.7, p: 0.034); incomplete vaccination scheme (OR: 2.3, 95% CI: 1.1-5.1: p: 0.015). There wasn't any statistically significant difference between sex and severe pneumonia; However, the male sex had a 50% higher risk (OR 1.59, CI: 0.73- 3.59, p: 0.13). History of overcrowding, exposure to smoke or biomass and asthma didn't show differences between patients with severe and very severe pneumonia.

Table 5. Risk factor for severity CAP at Napoleón Franco Pareja Children's Hospital in 2014

Risk factor		CAP Severe		CAP Very severe		Total		Pr(X2)	OR	CI95% Lower	CI95% Upper	P
		n	%	n	%	n	%					
Sex	Male	137	51,5	22	62,9	159	52,82	0,21	1,59	0,73	3,59	0,139
	Female	129	48,5	13	37,1	142	47,18					
Age <= 3 month	Yes	13	4,9	7	20,0	20	6,64	0,00	4,87	1,50	14,36	0,004
	No	253	95,1	28	80,0	281	93,36					
Mother's age <20 years	Yes	64	24,1	9	25,7	73	24,25	0,83	1,09	0,43	2,56	0,487
	No	202	75,9	26	74,3	228	75,75					
Breastfeeding <6 moths	Yes	117	44,0	25	71,4	142	47,18	0,00	3,18	1,40	7,71	0,002
	No	149	56,0	10	28,6	159	52,82					
Mother with no education	Yes	2	0,8	1	2,9	3	1	0,02	3,88	0,06	75,89	0,311
	No	264	99,3	34	97,1	298	99					
Incomplete vaccination	Yes	97	36,5	20	57,1	117	38,87	0,02	2,32	1,07	5,11	0,016
	No	169	63,5	15	42,9	184	61,13					
Overcrowding	Yes	96	36,2	13	37,1	109	36,33	0,92	1,04	0,46	2,27	0,527
	No	169	63,8	22	62,9	191	63,67					
Malnutrition	Yes	14	5,3	4	11,4	18	5,98	0,15	2,32	0,52	8,00	0,143
	No	252	94,7	31	88,6	283	94,02					
Exposure to tobacco	Yes	25	9,4	3	8,6	28	9,3	0,87	0,90	0,17	3,23	0,585
	No	241	90,6	32	91,4	273	90,7					
Exposure to smoke	Yes	52	19,6	11	31,4	63	20,93	0,10	1,89	0,78	4,30	0,084
	No	214	80,5	24	68,6	238	79,07					
Cardiopathy	Yes	8	3,0	5	14,3	13	4,32	0,00	5,38	1,29	19,89	0,010
	No	258	97,0	30	85,7	288	95,68					
Late medical consultation	Yes	86	32,3	10	28,6	96	31,89	0,65	ND			
	No	180	67,7	25	71,4	205	68,11					
Asthma	Yes	94	35,3	10	28,6	104	34,55	0,43	0,73	0,30	1,66	0,277
	No	172	64,7	25	71,4	197	65,45					
Allergies	Yes	15	5,6	0	-	15	4,98	0,15	ND			
	No	251	94,4	35	100,0	286	95,02					
Diabetes	Yes	3	1,1	0	-	3	1	0,53	ND			
	No	263	98,9	35	100,0	298	99					
Down	Yes	1	0,4	0	-	1	0,33	0,72	ND			
	No	265	99,6	35	100,0	300	99,67					
Sickle cell anemia	Yes	10	3,8	1	2,9	11	3,65	0,79	0,75	0,02	5,60	0,627
	No	256	96,2	34	97,1	290	96,35					

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Risk factor		CAP Severe		CAP Very severe		Total		Pr(X2)	OR	CI95% Lower	CI95% Upper	P
		n	%	n	%	n	%					
Prematurity	Yes	27	10,2	8	22,9	35	11,63	0,03	2,62	0,93	6,69	0,034
	No	239	89,9	27	77,1	266	88,37					
Hospitalised with CAP	Yes	10	3,8	1	2,9	11	3,65	0,79	0,75	0,02	5,60	0,627
	No	256	96,2	34	97,1	290	96,35					
Exposure to painting	Yes	8	3,0	0	-	8	2,66	0,30	ND			
	No	258	97,0	35	100,0	293	97,34					
Others	Yes	29	10,9	9	25,7	38	12,62	0,01	2,83	1,06	6,98	0,019
	No	237	89,1	26	74,3	263	87,38					

Microbiological profile

5% of the 180 blood cultures performed were positive. The most frequent germ isolated was S. pneumoniae with 5 cases, 4 of them were admitted in ICU: 1 had not vaccination against pneumococcus, 2 received breastfeeding less than 6 months, one had sickle cell anemia and heart disease. Four had a pleural effusion and two presented sepsis as complications too. The virological tests carried out, were positive so: 4.5% for influenza A, 4.4% for influenza B, 14% for H1N1 and 36.5% for RSV (Table 6).

Table 6. CAP microbiological profile at Napoleón Franco Pareja Children's Hospital in 2014

	N=301	%
Blood cultures	180	59,8
Positive	9	5,0
E.coli	1	11,1
Micrococus	1	11,1
S. Aureus	1	11,1
S. Pneumoniae	5	55,5
S. Epidermidis	1	11,1
Viral panel made	44	14,6
Influenza A	44	14,6
Negative	42	95,5
Positive	2	4,6
Influenza B	45	14,9
Negative	43	95,6
Positive	2	4,4
H1N1	50	16,6
Negative	43	86,0
Positive	7	14,0
RSV	52	17,3
Negative	33	63,5
Positive	19	36,5

Continúa...

Discussion

This study analyzes the socioeconomic, epidemiological, clinical characteristics and most frequent complications found in children with severe and very severe CAP in a pediatric hospital, and their relationship with risk factors associated with this clinical evolution.

The WHO and the British Chest Society define CAP as the presence of tachypnea associated with symptoms of fever, cough and chest wall indrawing(26, 27). Tachypnea occurs due to activation of an inflammatory cascade induced by a germ that alters gas exchange

at the alveolocapillary level; When it is not compensated, it evolves to chest retractions, nasal flaring, whining, signs of shock and ventilatory failure with a high risk of death. (28).

Shann, Spooner and Levental's studies showed that the tachypnea and chest wall indrawing as diagnostic signs established by the WHO have high predictive value in children less 2 years old. (29, 30). However, in our study, 30.9% of the children didn't present tachypnea, but radiological findings and complications such as pleural effusion were found in them, which is consistent with other established consensus such as the American Society of Infectious Diseases, which defines CAP as the presence of signs and symptoms of pneumonia that can be confirmed by findings of infiltrates in chest X-rays, in previously healthy children acquired before hospital admission (31).

Only 66.5% of studied children presented chest wall indrawing, that indicates it shouldn't be considered as the only criterion of severity. Other findings such as cyanosis, oxygen therapy, complicated pneumonia or the presence of highly virulent germs such as S. aureus are also included in this concept (27, 31).

Majorities of CAP are managed ambulatorily, but if there is any criterion of severity such as: respiratory distress, oxygen requirement, intolerance to the oral route, cyanosis, chest wall indrawing, to be less than 3 months old is considered hospital treatment. The subjects studied had some of these conditions, because of that, they were classified as severe pneumonia (88.7%).

Patients with CAP who present imminent signs of ventilatory failure, hemodynamic instability, needing for ventilatory and / or inotropic support are classified as very severe pneumonia and require ICU treatment (32). In our study, ten of the patients classified in this category didn't present complications associated with shock or these supports. However, they were at risk of ventilatory failure requiring continuous monitoring, which explains their admission to the ICU (32).

In our study, complications from CAP were presented independently of their severity; the risk of complications in very severe CAP was higher, sepsis and atelectasis were more common in this group. Although the development of empyema in comparison with other complications wasn't as relevant, it was more common in very severe CAP with a statistically significant difference ($p = 0.041$).

Pneumonia cases increase in the rainy season, due to the spread of respiratory pathogens from person to person, and the dryness of mucous membranes is facilitated, which alters their mucociliary function (15). In 2014, pneumonia cases occurred throughout the year, with peaks between June and July and in November, which could be associated with increased rains during these dates.

Although belonging to the male sex is associated with severity (33), In our study there were no differences in relation to sex. Being younger than 3 months or premature, were common factors in these children and coincides with the risk of severity described in the literature.

Breast milk is rich in secretory IgA that prevents the adherence of viruses and bacteria to the respiratory mucosa, so its exclusive consumption during the first 6 months of life is a protective factor (15, 25). In this sample, it was found that not having this condition tripled the risk of severity. When severe malnutrition

occurs, the immune response decreases, facilitating the development of severe CAP (12). In our population, malnutrition doubled the risk of severity (OR 2.32, 95% CI: 0.52-8.00, p: 0.14), including death, evidenced in two cases.

Comorbidities like sickle cell anemia, bronchopulmonary dysplasia, gastroesophageal reflux, asthma, cystic fibrosis, congenital heart disease or immunodeficiency are associated to complications and neuromuscular disease and epilepsy to aspiration pneumonia(34). In our study, heart disease was associated with very severe pneumonia (p 0.010); However, asthma or sickle cell anemia did not increase the risk of admission to the ICU due to very severe pneumonia, it's possible that the presence of other factors that increase this risk may be required.

Active vaccination has been considered a significant resource to reduce morbidity and mortality by CAP (15). Studies describe that immunization against *Haemophilus influenza* and *S pneumoniae* reduced the radiological incidence of CAP by 20%(35). Incomplete vaccination was associated with severe pneumonia in our population.

Environmental contamination and exposure to smoke or biomass, block the mucociliary response of the respiratory tract (15). Overcrowding (12) facilitates nasopharyngeal colonization of germs, this and the late consultation (24) are associated with risk of severity. In our study, there were no differences between severe and very severe CAP when these factors were associated.

It is known that it is difficult to determine the etiological agent of pneumonias in the world (19, 20). Blood cultures are positive in less than 10% of cases (21, 22). In our study, only 5% of the blood cultures were positive. The most frequent isolated germ was S. pneumoniae, which was associated with very severe pneumonia and complications, but not death. Despite the expectation that these cases had a history of incomplete vaccination for pneumococcus, only one met this criterion. This suggests that it is possible that the strain present in these cases isn't covered by the vaccine. New studies should be carried out to establish the pneumococcal subtype in this population and correlate it with those present in the vaccine applied by the EPI.

CONCLUSIONS

CAP is one of the infectious causes with greater morbidity and mortality in our environment. It can be associated to risk factors that predispose to the development of severity. In our study, we found exclusive breastfeeding for under six months since birth, prematurity, heart disease, incomplete vaccination and blood cultures positive for S. pneumoniae increased risk of significant severity. Working on measures that modify these risk factors could reduce complications, hospital staying and death, which in turn would reduce costs. For this reason, the training of health personnel and the vulnerable population is essential.

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